

ALT-836 Fact Sheet



ALT-836 is a novel, high-affinity, chimeric anti-tissue factor monoclonal antibody that binds to human tissue factor (TF) or the TF-Factor VIIa (FVIIa) complex preventing binding and activation of Factor X (FX) and Factor IX (FIX) to inhibit thrombin generation [1]. It is in a Phase 2 trial for treatment of patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). Currently, there is no approved pharmacotherapy for treating these high-mortality diseases. Estimates of the health-care costs associated with ALI/ARDS may exceed \$5 billion per year just in the US. Therefore, an effective therapeutic will significantly reduce the high

mortality rate and tremendous health-care costs associated with ALI/ARDS by shortening the ventilation time and the duration of ICU stay.

TF is a membrane protein that initiates the extrinsic coagulation pathway, with important additional roles in tumor growth, angiogenesis, and inflammation. There is an abundance of published evidence that coagulation and inflammation processes are closely related in the pathology of ALI/ARDS and tumor metastasis, suggesting that TF antagonists could be effective in treating these diseases. Numerous studies conducted at Altor, using ALT-836, and other laboratories, employing other TF antagonists, have confirmed these suggestions.

In the Proximate-TIMI 27 trial in patients with coronary artery diseases and in two non-human primate models [1-3], ALT-836 was shown to have favorable pharmacokinetic and safety profiles. ALT-836 also exhibits potent activity for blocking thrombin generation and relevant clinical activities without compromising hemostasis. The safety profile of ALT-836 was further confirmed in a Phase 1/2a trial in patients with ALI/ARDS, a population prone to having serious bleeding episodes. In 2009, Altor initiated a multi-center, randomized, placebo-controlled Phase 2 clinical trial of ALT-836 in ALI/ARDS patients. Sixty patients were enrolled and interim analysis indicates favorable safety and clinical benefits to patients receiving a single-dose of ALT-836. This study was supported by a Phase II SBIR grant from National Heart Lung and Blood Institute (NHLBI)

A second Phase 2, 90-patient trial is underway using a multi-dose regimen to further evaluate safety and efficacy of ALT-836 (<http://clinicaltrials.gov/NCT00879606>). The trial is projected to conclude in early 2012. Favorable efficacy will prompt a Phase 3 study of ALT-836 for product approval. In addition, favorable anti-inflammatory results and safety profile using a multi-dose regimen from this Phase 2 trial will open the potential of employing ALT-836 for treatment of other systemic inflammatory diseases, such as colitis and autoimmune diseases. This second Phase 2 trial is supported by a recently awarded Competing Renewal SBIR grant from NHLBI.

TF is known to play a major role in cancer metastasis and angiogenesis. In pre-clinical studies, ALT-836 exhibits potent anti-tumor, anti-angiogenic, and anti-metastasis activities. Altor has initiated a clinical trial for ALT-836 against solid tumors that overexpress TF, such as non-small cell lung cancer, soft tissue sarcoma and pancreatic cancer, which are known to have related coagulopathies for which ALT-836 may have benefit. Patient enrollment is underway for this Phase 1 trial of ALT-836 in combination with gemcitabine in patients with locally advanced or metastatic solid tumors (<http://clinicaltrials.gov/NCT01325558>).

Altor and Genentech are collaborating on ALT-836 development. A robust combined patent portfolio on monoclonal antibody-based TF antagonists protects ALT-836.

The following publications can be provided and sent as e-mail attachments:

1. Jiao, J.A., et al., *Inhibition of acute vascular thrombosis in chimpanzees by an anti-human tissue factor antibody targeting the factor X binding site*. *Thromb Haemost*, 2010. **103**(1): p. 224-33.
2. Welty-Wolf, K.E., et al., *Blockade of tissue factor-factor X binding attenuates sepsis-induced respiratory and renal failure*. *Am J Physiol Lung Cell Mol Physiol*, 2006. **290**(1): p. L21-31.
3. Morrow, D.A., et al., *Potent inhibition of thrombin with a monoclonal antibody against tissue factor (Sunol-cH36): results of the PROXIMATE-TIMI 27 trial*. *Eur Heart J*, 2005. **26**(7): p. 682-8.

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